

IN THE CLAIMS:

Please amend claim 1 as follows:

1. (PRESENTLY AMENDED) A multiparticulate bisoprolol formulation for once-daily oral administration, said formulation comprising at least two particles comprising a core of bisoprolol or a pharmaceutically acceptable salt thereof, and a polymeric coating comprising at least one polymer that exhibits a pH-dependent dissolution profile and imparts a pH-dependent ~~and pH independent~~ delay in bisoprolol release, wherein following administration said formulation exhibits a lag in release, producing a bisoprolol plasma concentration of not more than about 1 ng/ml for at least about three hours, and thereafter provides a sustained release of bisoprolol that produces a therapeutic plasma concentration not later than about 12 hours following administration, and wherein said formulation maintains a therapeutic plasma concentration of bisoprolol for the remainder of a twenty-four hour period measured from administration.

2. (Cancelled)

3. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 1, comprising a pharmaceutically acceptable salt of bisoprolol.

4. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 3, wherein the bisoprolol salt is bisoprolol hemifumarate.

5. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 1, which, when measured in a U.S. Pharmacopoeia 2 Apparatus (Paddles) in phosphate buffer at pH 6.8 at 37°C and 50 rpm, exhibits a dissolution profile substantially corresponding to the following:

- (a) from 0% to 10% of the total bisoprolol is measured after 2 hours in said apparatus;
- (b) from 0% to 50% of the total bisoprolol is measured after 4 hours in said apparatus; and
- (c) greater than 50% of the total bisoprolol is measured after 10 hours in said apparatus.

6. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 1, which, when measured in a U.S. Pharmacopoeia 1 Apparatus (Baskets) at 37°C and 50 rpm in 0.01 N HCl for the first 2 hours followed by transfer to phosphate buffer at pH 6.8 for the remainder of the measuring period, exhibits a dissolution profile substantially corresponding to the following:

- (a) from 0% to 10% of the total bisoprolol is measured after 2 hours in said apparatus;
- (b) less than 50% of the total bisoprolol is measured after 4 hours in said apparatus; and
- (c) greater than 20% of the total bisoprolol is measured after 10 hours in said apparatus.

7. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein at least two particles comprise a sealant or barrier layer between the core and the polymeric coating.

8. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 7, wherein the sealant or barrier layer comprises at least one of hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxypropyl ethylcellulose or xanthan gum.

9. (CANCELLED)

10. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one pharmaceutically acceptable film-forming polymer that forms an insoluble film of low permeability and wherein said at least one polymer that forms an insoluble film of low permeability comprises from about 80 to about 100 percent of the polymers in said coating.

11. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 10, wherein the polymeric coating comprises at least one pharmaceutically acceptable film-forming polymer that forms an insoluble film of high permeability comprises from about 0 to about 20 percent of the polymers in said coating.

12. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 10, wherein the polymeric coating comprises a methacrylic acid co-polymer.

13. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 10, wherein the polymeric coating comprises an ammonio methacrylate co-polymer.

14. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 12, wherein the polymeric coating comprises a mixture of methacrylate co-polymers and ammonio methacrylate co-polymers.

15. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one soluble excipient.

16. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 15, wherein the soluble excipient is chosen from

soluble, polymers, surfactants, alkali metal salts, organic acids, sugars, and sugar alcohols.

17. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 15, wherein the soluble excipient is chosen from polyvinyl pyrrolidone, polyethylene glycol, and mannitol.

18. (PREVIOUSLY AMENDED) The Multiparticulate bisoprolol formulation according to claim 15, wherein the soluble excipient is present in an amount of from 1% to 10% by weight, based on the total dry weight of polymer in the polymeric coating.

19. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises one or more auxiliary agents chosen from fillers, plasticizers, and anti-foaming agents.

20. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating produce a weight gain of from about 10% to 100% to the core.

21. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 20, wherein the polymeric coating produce a weight gain of from about 25% to 70 % to the core.

22. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein a sealant or barrier is applied to the polymeric coating.

23. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 22, wherein the sealant or barrier comprises at least one of hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxypropyl ethylcellulose or xanthan gum.

24. (PREVIOUSLY AMENDED) An oral dosage form comprising a multiparticulate bisoprolol formulation according to claim 1, which is in the form of caplets, capsules, particles for suspension, sachets, or tablets.

25. (PREVIOUSLY AMENDED) The oral dosage form according to claim 24, which is in the form of tablets chosen from disintegrating tablets, fast dissolving tablets, effervescent tablets, fast melt tablets, and mini-tablets.

26. (CANCELLED)

27. (CANCELLED)

28. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 11, wherein the polymeric coating comprises a methacrylic acid co-polymer.

29. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 11, wherein the polymeric coating comprises an ammonio methacrylate co-polymer.

30. (PREVIOUSLY AMENDED) The multiparticulate bisoprolol formulation according to claim 11, wherein the polymeric coating comprises a mixture of methacrylate co-polymers and ammonio methacrylate co-polymers.

31. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one polymer that dissolves in a pH-dependent manner.

32. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 31, wherein the formulation releases bisoprolol in a manner that is dependent on the local pH of the gastrointestinal tract.

33. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one polymer that dissolves in a pH-independent manner.

34. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 33, wherein the formulation releases bisoprolol in a manner that is independent of the local pH of the gastrointestinal tract.

35. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 1, wherein the formulation provides a sustained

release of bisoprolol that produces a therapeutic plasma concentration not later than about 6 hours following administration.

36. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 1, wherein the formulation further comprises talc.

37. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 1, wherein the formulation comprises a substantially purified enantiomer of bisoprolol.

38. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 37, wherein the substantially purified enantiomer of bisoprolol is (S)-bisoprolol.

39. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 37, wherein the substantially purified enantiomer of bisoprolol is (R)-bisoprolol.

40. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one pharmaceutically acceptable film-forming polymer that forms an insoluble film of low permeability.

41. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 40, wherein the polymeric coating further

comprises at least one pharmaceutically acceptable film-forming polymer that forms an insoluble film of high permeability.

42. (PREVIOUSLY PRESENTED) The multiparticulate bisoprolol formulation according to claim 40, wherein at least one pharmaceutically acceptable film-forming polymer that forms an insoluble film of low permeability is present in an amount greater than the amount of any pharmaceutically acceptable film-forming polymers that form an insoluble film of high permeability.